

REMARKS

Claims 1-11 were pending in the application; with the present amendment adding new Claims 12-24, Claims 1-24 are now pending. Claims 1-11 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Varma et al, U.S. Patent No. 5,622,826 (hereafter "Varma"). Claims 1-11 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Bamdad et al, U.S. Patent No. 5,620,850 (hereafter "Bamdad"). Claims 1-11 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Hefti, U.S. Patent Application Publication No. 2002/0009723 (hereafter "Hefti"). In addition, Claims 3 and 7 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Hefti in view of Ribí et al., U.S. Patent No. 5,491,097 (hereafter "Ribí"). Applicants respectfully traverse the rejections in view of the arguments and amendments presented herein.

The amendments to the claims find support in the specification and claims as originally filed. No new matter is added by way of the amendments. A heterobifunctional spacer having a biotinamide soft base is disclosed in Example 1 and in Figure 1. A heterobifunctional spacer having an iodoacetyl moiety soft base is disclosed in Example 3 and in Figure 3. Thus, with respect to the amendments to Claims 1 and 5, support for heterobifunctional spacers that include biotinamide or iodoacetyl moieties may be found in Example 1 (e.g., page 12, lines 4-5), Example 3 (e.g., page 14, line 11) and in Figures 1 and 3. Support for the amendments to Claims 4 and 8 may be found in Example 1 (e.g., page 12, lines 4-5) and Figure 1.

New Claims 12-24 are not disclosed or suggested in the prior art. For example, new Claims 12 and 13 recite a heterobifunctional spacer that is succinimidyl 6-[6-(((iodoacetyl)amino)-hexanoyl)amino]hexanoate that is novel and unsuggested by the prior art. Support for new Claims 12 and 13 may be found in Example 3 (e.g., page 14, line 11) and Figure 3.

New Claims 14-21 recite a heterobifunctional spacer having at least two functional groups including a soft base and an N-hydroxy succinimide ester. Support for new Claims 14-21 may be found in original Claims 1-11, (e.g., original Claims 1 and 5)

and in the specification. For example, support for a spacer with functional groups including a soft base and an N-hydroxy succinimide ester is found in the specification as originally filed, for example, at page 4, lines 18-26; page 7, lines 21-28; page 10, Table 2; the Examples; and elsewhere in the specification, claims and figures. Support for the spacer being chemi- or physisorbed to a soft metal solid support via soft metal-soft base bonding wherein the soft base is selected from the group consisting of RSH, RS⁻, R₂S, RSSR, CN⁻, S₂O₃²⁻, I⁻, R₃P, (RO)₃P, C₂H₄ and C₆H₆ group, where R is an organic group, may be found at page 4, lines 24-25. Such heterobifunctional spacers are novel and unsuggested by the prior art.

In addition, new Claims 22-24 recite methods for recovering ligands immobilized on a silver-containing support by an iodine-containing heterobifunctional spacer, including steps of contacting the support with a thiodyglycol solution, and of exposing the support and thiodyglycol solution to ultrasonic energy, that are novel and unsuggested by the prior art. Support for new Claims 22-24 may be found in Example 4 (page 15, lines 6-23).

The Rejections of Claims 1-11 Under 35 U.S.C. §102(b) Over Varma

Claims 1-11 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Varma et al, U.S. Patent No. 5,622,826 (hereafter "Varma"). Applicants respectfully traverse this rejection.

Anticipation under 35 U.S.C. §102 requires that "every element of the claimed invention be identically shown in a single reference." (*In re Bond*, 910 F.2d 831,832 (Fed. Cir. 1990).

Varma suggests that molecules having an amino group or functionality may be "immobilized on platinum surfaces by first reacting such surfaces with either an isocyanate or an isothiocyanate" (column 2, lines 51-53). However, Varma nowhere discusses reacting a surface with a biotinamide or with an iodoacetyl moiety, nor in particular, with succinimidyl-6-(biotinamido)hexanoate or with succinimidyl 6-[6-(((iodoacetyl)amino)-hexanoyl)amino]hexanoate. Moreover, Varma fails to discuss reacting a surface with a heterobifunctional spacer having at least two functional groups

including a soft base and an N-hydroxy succinimide ester, the soft base being selected from the group consisting of RSH, RS⁻, R₂S, RSSR, CN⁻, S₂O₃²⁻, I⁻, R₃P, (RO)₃P, C₂H₄ and C₆H₆ group, where R is an organic group.

Accordingly, the cited reference lacking at least these elements of the claimed invention, Applicants believe the rejection of Claims 1-11 under 35 U.S.C. §102(b) over Varma to be overcome.

The Rejections of Claims 1-11 Under 35 U.S.C. §102(b) Over Bamdad

Claims 1-11 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Bamdad et al, U.S. Patent 5,620,850 (hereafter "Bamdad"). Applicants respectfully traverse this rejection.

The Examiner presents Bamdad as providing X-R-Ch-M-BP-Bmol, in which X represents a functional group that adheres to a gold surface, and in which X "can be thiols, sulfide, disulfide, and the like" (Paper No. 8, page 3, lines 11-14). However, Claims 1-11 are directed to subject matter that is not discussed in Bamdad.

Bamdad nowhere discusses a reagent for reacting with a surface that includes a biotinamide or an iodoacetyl moiety, nor in particular, that includes succinimidyl-6-(biotinamido)hexanoate or succinimidyl 6-[6-(((iodoacetyl)amino)-hexanoyl)amino]hexanoate. Moreover, Bamdad fails to discuss or heterobifunctional spacers having at least two functional groups including a soft base and an N-hydroxy succinimide ester for reacting with a soft base including moieties selected from the group consisting of RSH, RS⁻, R₂S, RSSR, CN⁻, S₂O₃²⁻, I⁻, R₃P, (RO)₃P, C₂H₄ and C₆H₆ group, where R is an organic group.

Accordingly, the cited reference lacking at least these elements of the claimed invention, Applicants believe the rejection of Claims 1-11 under 35 U.S.C. §102(b) over Bamdad to be overcome.

The Rejections of Claims 1-11 Under 35 U.S.C. §102(e) Over Hefti

Claims 1-11 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by Hefti, U.S. Patent Application Publication No. 2002/0009723 (hereafter "Hefti"). Applicants respectfully traverse this rejection.

The Examiner suggests that Hefti discusses as assay system including a ligand binding surface with a soft metal support, and discusses heterobifunctional linkers and attachment chemistry (Paper No. 8, pages 3-4).

However, Hefti nowhere discusses reacting a soft metal surface with a heterobifunctional linker that includes a biotinamide or that includes an iodoacetyl moiety, nor in particular, that includes succinimidyl-6-(biotinamido)hexanoate or succinimidyl 6-[6-(((iodoacetyl)amino)-hexanoyl)amino]hexanoate. Moreover, Hefti fails to discuss heterobifunctional spacers having at least two functional groups including a soft base and an N-hydroxy succinimide ester for reacting with a soft metal surface including moieties selected from the group consisting of RSH, RS⁻, R₂S, RSSR, CN⁻, S₂O₃²⁻, I⁻, R₃P, (RO)₃P, C₂H₄ and C₆H₆ group, where R is an organic group.

Accordingly, the cited reference lacking at least these elements of the claimed invention, Applicants believe the rejection of Claims 1-11 under 35 U.S.C. §102(e) over Hefti to be overcome.

The Rejections of Claims 3 and 7 Under 35 U.S.C. §103(a)

Claims 3 and 7 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Hefti in view of Ribí et al, U.S. Patent No. 5,491,097 (hereafter "Ribí"). Applicants respectfully traverse this rejection.

In order to establish a prima facie case of obviousness, there must be: 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art,

and not based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Hefti is presented by the Examiner to provide elements discussed above. As noted by the Examiner, Hefti lacks disclosure regarding heterobifunctional linkers comprising a hydrocarbon of about 10 to about 40 atoms in length (Paper No. 8, page 5, lines 8-9). Ribí is presented to provide such linkers. However, Ribí does not discuss linkers of up to about 40 carbons, discussing at most 30 carbons (Ribí, column 5, line 50). Moreover, Ribí does not discuss linkers attaching to a metal substrate, as required by the present claims, and so does not bear on the present invention.

However, regardless of the length of a hydrocarbon portion of a heterobifunctional linker, even if taken together Hefti and Ribí fail to provide all the elements of the claimed invention, the combination failing to disclose at least the elements of a heterobifunctional linker that includes a biotinamide or an iodoacetyl moiety; failing to provide either succinimidyl-6-(biotinamido)hexanoate or succinimidyl 6-[6-(((iodoacetyl)amino)-hexanoyl)amino]hexanoate linkers; and failing to provide heterobifunctional spacers having at least two functional groups including a soft base and an N-hydroxy succinimide ester for reacting with a soft metal surface including moieties selected from the group consisting of RSH, RS⁻, R₂S, RSSR, CN⁻, S₂O₃²⁻, I⁻, R₃P, (RO)₃P, C₂H₄ and C₆H₆ group, where R is an organic group.

In addition, there is no motivation or suggestion in Hefti or in Ribí to combine them to provide the missing elements. Ribí is not directed to attachment of ligands to metal surfaces, and so would not be combined with a reference in order to provide means to do so. Even were such a combination to be made, the references do not provide a reasonable expectation of success for providing the claimed invention, since the references fail to discuss the missing elements and thus provide no expectation of success for an invention requiring those elements.

Thus, since the cited references do not disclose the claimed heterobifunctional linkers, do not disclose the claimed linkage via soft metal-soft base bonding, provide no motivation to combine the cited references to provide the claimed invention, nor any

reasonable expectation of success were the references to be so combined, Applicants respectfully submit that Claims 1-11 are not made obvious by the cited references.

Accordingly, Applicants believe the rejection of Claims 1-11 under 35 U.S.C. §103(a) over Hefti in view of Ribí to be overcome.

CONCLUSION

Applicants respectfully request consideration and allowance of all pending claims. The Examiner is invited to contact the undersigned attorney at the telephone number indicated below should he find that there are any further issues outstanding.

Please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **25527-0001**.

Respectfully submitted,

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